REMARKS

Applicant thanks Examiner Bristol for the telephone conference held on July 18, 2007 with Applicants' representative, Kelli Watson Francuzenko, to discuss the issues outstanding in the present final Office Action, mailed January 22, 2007.

Applicant has amended the specification to correct a typographical error in the spelling of the toxin named "restrictocin." One of skill in the art would have appreciated that the specification incorrectly spelled this toxin. Accordingly, Applicant submits that the amendment does not constitute new matter and respectfully requests entry of the amendment.

Claims 11-26 are pending in the present application. In order to expedite prosecution of the application and without conceding to the propriety of the rejections, Applicant has amended claims 11, 13, 16, and 19-26. Applicant has also added new claims 27-89.

Support for the claim amendments and new claims can be found in the specification as originally at, *e.g.*, page 3, *l.* 9 to page 4, *l.* 2; page 4, *ll.* 8-10 and *ll.* 15-20; page 6, *ll.* 10-12; page 6, *l.* 29 to page 7, *l.* 15; page 13, *ll.* 9-26; page 14, *l.* 22 to page 15, *l.* 8; page 16, *ll.* 22-23; page 16, *l.* 32 to page 17, *l.* 35; page 20, *ll.* 10-11; page 20, *l.* 32 to page 21, *l.* 2; page 23, *ll.* 30-32; and page 25, *ll.* 9-10. Thus, the claim amendments and new claims do not constitute new matter. Claims 11-89, therefore, will be pending upon entry of this Amendment.

Applicant respectfully requests that the remarks and amendments be considered and made of record in the present application.

I. The Rejections Under 35 U.S.C. § 112, First Paragraph, For Lack of Written Description Should be Withdrawn

Claims 11-26 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. The gravemen of this rejection is that certain claim recitations (specified below) are not sufficiently described in the specification as to convey possession of the invention at the filing of the application. For the reasons below, the rejections under 35 USC § 112, first paragraph, for lack of written description should be withdrawn.

The factual inquiry for assessing sufficiency of the written description under 35 U.S.C. § 112 is whether the specification conveys with reasonable clarity to those skilled in the art that the applicant was in possession of the claimed invention as of the filing date. *Vas-*

Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ 2d 1111, 1117 (Fed. Cir. 1991). What is required is that the description clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed. See *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996) ("*ipsis verbis* disclosure is not necessary to satisfy the written description requirement of section 112. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the subject matter in question."). Disclosure of sufficiently detailed, relevant identifying characteristics, *i.e.*, structure, physical, and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or combination of such characteristics can provide evidence that the applicant was in possession of the claimed invention. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d at 964, 63 USPQ2d at 1613 (Fed. Cir. 2002). Under these principles, the claim recitations in question are adequately supported within the meaning of the written description requirement of 35 U.S.C. § 112.

The Examiner alleges that the specification does not provide written description support for the recitation "cell that expresses CD132." Applicant has amended claims 11, 16 and 22-24 to correct the typographical error in the name of the antigen. The claims now recite the correct name of the antigen, namely CD123. Support in the specification for the antigen can be found, *e.g.*, at page 3, *ll.* 9-14. Applicant believes that the amendment overcomes the Examiner's rejection and requests that the rejection be withdrawn.

The Examiner also alleges that the specification does not provide written description support for the recitation "does not significantly express CD131." The present specification describes that CD123 was detectable on certain hematologic cancer progenitor cells but that CD131 was not detectable as assessed by flow cytometry (see, *e.g.*, page 23, *ll.* 30-32 of the specification). Applicant submits that one of skill in the art reading the specification would appreciate that the invention includes hematologic cancer progenitor cells that do not significantly express CD131. Therefore, the rejection for lack of written description should be withdrawn.

II. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should be Withdrawn

Claims 11-26 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. For the reasons detailed below, the rejections under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

The Examiner alleges that claims 11 and 22 are indefinite because it is unclear how much of an "amount effective" is required to achieve the effect. Applicant has amended claims 11 and 22 so that they no longer recite that compositions comprise an amount effective to achieve a particular effect. Applicant respectfully submits that the claim amendments obviate the Examiner's rejection and request that the rejection be withdrawn.

The Examiner alleges that claim 16 is indefinite because the following recitations are unclear "component of the sample" and "compound." Applicant has amended claim 16 so that it longer contains these recitations. Applicant respectfully submits that the claim amendments obviate the Examiner's rejection and request that the rejection be withdrawn.

The Examiner alleges that claims 11-26 are indefinite because the specification does not define what the amount of CD131 would be to determine that a cell "does not significantly express CD131." The present specification teaches that CD131 is not detectable by flow cytometry and describes this techniques (see, *e.g.*, page 21, *ll.* 22-36 and page 23, *ll.* 30-32 of the specification). Applicant respectfully submits that one of skill in the art would understand the recitation "does not significantly express CD131" to mean that the cells do not express a detectable amount of CD131 as measured by a technique in the art, such as flow cytometry. Thus, Applicant submits that one of skill in the art could readily determine whether a cell does not significantly express CD131 using, *e.g.*, the flow cytometry technique described in the specification. Accordingly, Applicant requests that the rejection be withdrawn.

III. The Pending Claims Are Patentable Over Broudy, Koubek, Voisin and Lopez

The pending claims are not anticipated or rendered obvious by Broudy et al., U.S. Patent No. 5,489,516 ("Broudy"), Koubek et al., 1999, Eur. J. Haematol. 63: 1-10 ("Koubek"), Lopez, International Publication No. WO 97/24373 ("Lopez"), or Voisin et al., U.S. Patent No. 4,340,535 ("Voisin").

1. The Pending Claims Are Novel

Neither Broudy, Koubek, Lopez nor Voisin anticipate the claimed invention. None of these references teach compositions that selectively bind to CD123 and are composed of a therapeutically effective amount of an antibody and a cytotoxic agent or the use of such a composition to treat a hematologic cancer or to selectively impair or purge cancer cells, in particular cancer progenitor cells, that express CD123 but do not significantly express

CD131. Further, none of these references teach detecting hematologic cancer progenitor cells that express CD123 but do not significantly express CD131.

For a prior reference to anticipate a claimed invention, the reference must disclose each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. *W.L. Gore Associates v. Garlock, Inc.*, 721 F.2d 1540, 1554 (Fed. Cir. 1983); *In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985). Neither Broudy, Koubek, Lopez nor Voisin describe each and every limitation of the claimed compositions and claimed methods. Broudy describes antibodies directed to a receptor for stem cell factor ("SCF") and uses of those antibodies. Koubek merely states that CD123 is expressed mostly on immature myeloid progenitor leukemia cells. Lopez describes an antibody directed to CD123 that acts as an antagonist to IL-3. Voisin describes a process for coupling the A chain of ricin with an antibody. Accordingly, the claimed compositions and methods are not anticipated by Broudy, Koubek, Lopez or Voisin.

2. The Pending Claims Are Not Obvious

As discussed above, the claimed invention relates to compositions comprising anti-CD123 antibodies coupled to cytotoxic agents present in therapeutically effective amounts to treat hematologic cancers, and methods of using such compositions in various treatment protocols. Neither Broudy, Koubek, Lopez nor Voisin, alone or in combination, render the claimed invention obvious.

None of the references taken alone or in combination describe or suggest the use of a cytotoxic agent specifically directed to a cell expressing CD123 as a means for the treatment of a hematologic cancer. Further, none of the references describe or suggest a therapeutically effective amount of an anti-CD123 antibody conjugated to a cytotoxic agent in the various treatment protocols claimed herein. In particular, Broudy describes the use of an antibody to a completely different and unrelated target, *i.e.*, SCF, and prophetically describes the use of such an antibody to treat cancer. The deficiencies in Broudy are not cured by combining the reference with Koubek, Lopez or Voisin.

Koubek describes a study in which the expression of a number of cytokine receptors, including CD123, by different lymphoid leukemic cells were assessed using monoclonal antibodies. There is no suggestion in Koubek that any of the targets reported would be useful

in a therapeutic context. Koubek, at best, suggests that the assays reported therein, not the antibodies, may have utility as research and diagnostic tools. Moreover, the antibodies reported in Koubek were unconjugated.

Further, Lopez, alone or in combination with Broudy and/or Koubek, does not render the claimed invention obvious. Lopez describes an antibody that binds to CD123 with the explicit purpose of blocking IL-3 activity. Lopez describes using a particular monoclonal antibody, namely MoAb 7G3, which although it recognizes CD123, was chosen in Lopez's study because it blocks IL-3 activity. According to Lopez, this particular antibody recognizes a very specific epitope which allows it to antagonize IL-3 activity. Thus, Lopez, at best, suggests inhibiting IL-3 activity for the treatment of cancer.

Voisin certainly does not cure the deficiencies of any of the references described above, as it merely provides general methods for coupling ricin A to an antibody. The mere fact that Voisin teaches general techniques for making such cytotoxic products would not have suggested to one of ordinary skill in the art to modify the teaching in Broudy, Koubek or Lopez to arrive at the claimed compositions, let alone the claimed methods.

Given the distinct functions of SCF receptors and CD123, one of ordinary skill would not have been motivated to combine the teachings of Broudy and Lopez to arrive at the claimed invention, nor would one of ordinary skill in the art have had a reasonable expectation of success. Koubek does not add anything to the teaching in Lopez regarding an antibody to CD123 or uses of such an antibody. Moreover, neither Lopez, Broudy or Koubek teach, suggest or even contemplate methods for detecting, purging or impairing cancer cells (in particular, hematologic cancer progenitor cells) that express CD123, but do not express CD131, using an antibody that selectively binds to CD123. Further, neither Lopez, Broudy or Koubek teach, suggest or even contemplate a composition that selectively binds to CD123 and that is composed of a therapeutically effective amount of an antibody and a cytotoxic agent, let alone methods for treating a hematologic cancer using such a composition.

In view of the foregoing, Applicant respectfully submits that neither Broudy, Koubek, Lopez nor Voisin, alone or in combination, render the claimed invention obvious.

CONCLUSION

Applicant respectfully requests that the above-made remarks and amendments be entered and made of record in the present application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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